

**REMARKS**

Claims 1, 3, 7, 8, and 14-17 are pending in this application. Non-elected claims 7 and 8 have been withdrawn from consideration by the Examiner. By this Amendment, claims 7 and 15 are amended, and claims 4-6 and 9-13 are canceled. Support for the amendments to the claims may be found, for example, in the specification. No new matter is added.

Entry of the amendments is proper under 37 CFR §1.116 because the amendments do not raise any new issues requiring further search and/or consideration:

- Withdrawn claim 7 is amended to include all the features of claim 1 to make claim 7 eligible for rejoinder should claim 1 be found allowable; and
- Claim 15 is amended to (1) address the claim objection/indefiniteness rejection set forth in the Office Action by replacing "amine compound" with "amine substance"; and (2) correct other informalities in claim 15 by deleting members of the Markush group that do not have "a boiling point of 50°C or higher and 300°C or lower" as required by claim 1 from which claim 15 depends.

Entry of these claim amendments was previously denied. *See* July 30 Advisory Action. In a telephone interview with SPE Lorengo inquiring why the amendments were not entered, SPE Lorengo explained that the rejection relied on the disclosure of tetramethylammonium hydroxide in the primary reference, and that cancellation of "tetraalkyl ammonium hydroxide" from claim 15 would require further search of the prior art for the other recited members of the Markush group.

In response, Applicants respectfully disagree with this basis. For the reasons previously made of record and the additional reasons presented below, the Office Action erroneously asserted that tetramethylammonium hydroxide has a boiling point within the claimed range. And, even though claim 1 uses the transitional phrase "comprising" and does not expressly exclude solutions as asserted by SPE Lorengo, claim 15 recites that the "amine

substance is selected from the group consisting of ...." Accordingly, the amine substance of claim 15 is limited to the specifically recited members, to the exclusion of all non-recited members. Thus, the "amine substance" of claim 15 as examined and rejected by the Office Action would not have read on a reference disclosing a solution of tetramethylammonium hydroxide and methanol.

In view of the foregoing amendments and following remarks, Applicants respectfully request reconsideration and allowance.

**I. Telephone Interview**

The courtesies extended to Applicants' representative by SPE Lorengo during the telephone interview held August 4, 2009, are appreciated. The reasons presented during the interview as warranting favorable action are incorporated into the remarks below, which constitute Applicants' record of the interview.

**II. Claim Objection**

The Office Action objects to claim 15 for an informality. Claim 15 is amended in light of the Examiner's helpful suggestion to replace "amine compound" with "amine substance." Accordingly, Applicants respectfully request reconsideration and withdrawal of the objection.

**III. Rejection under 35 U.S.C. §112, Second Paragraph**

The Office Action rejects claim 15 as being indefinite under 35 U.S.C. §112, second paragraph. By this Amendment, claim 15 is amended in light of the Examiner's comments. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

**IV. Double Patenting**

The Office Action objects to claim 9 as being a substantial duplicate of claim 3. By this Amendment, claim 9 is canceled, rendering its objection moot.

**V. Rejection Under 35 U.S.C. §103**

The Office Action rejects claims 1, 3, 9, and 14-17 under 35 U.S.C. §103(a) over U.S. Patent No. 6,941,572 to Horie et al. ("Horie") in view of U.S. Patent No. 6,337,060 to Hiraki et al. ("Hiraki") as evidenced by Perry's Handbook of Chemistry ("Perry's"). By this Amendment, claim 9 is canceled, rendering its rejection moot. As to the remaining claims, Applicants respectfully traverse the rejection.

The combination does not teach, suggest, or establish a reason or rational for providing "an amine substance having a boiling point of 50°C or higher and 300°C or lower" as claimed.

Horie discloses a suspension that includes tetramethylammonium hydroxide. Horie does not disclose any other amine substance dispersed in the suspension containing fine diamond particles. The Office Action asserts that tetramethylammonium hydroxide has a boiling point within the claimed range, relying on Perry's. *See* Office Action at page 5.

The Office Action's reliance on Perry's is improper. Perry's is a Material Safety Data Sheet (MSDS) for a composition comprising tetramethylammonium hydroxide, methanol, and optionally water. As would be clearly evident to one of skill in the art, this is not the same as tetramethylammonium hydroxide, and the properties of tetramethylammonium hydroxide in methanol cannot be used to evidence the properties of tetramethylammonium hydroxide compound. In fact, tetramethylammonium hydroxide has no boiling point, and dissolving the same into any solvent cannot impart a boiling point to tetramethylammonium hydroxide.

The Advisory Action asserts that "the information in the MSDS makes is [sic] clear that it's the boiling point of said amine compound that is within 60-65C and not the boiling point of methanol." Applicants disagree. In fact, the MSDS indicates "Boiling Point: 60 - 65C" without specifying that this is the boiling point of the amine substance and not the

methanol. Immediately below this it indicates "Melting Point: 63C" without specifying which component it is referring to. However, the Merck Index indicates that tetramethylammonium hydroxide has a melting point of 63°C and no boiling point, as tetramethylammonium hydroxide decomposes to trimethylamine and CH<sub>3</sub>OH upon distillation. *See* Tetramethylammonium hydroxide, The Merck Index, 7<sup>th</sup> Ed., page 1025 (submitted previously). The Merck Index indicates that methanol has a melting point of -97.8°C and a boiling point of 64.7°C. *Id.* at pages 1018-1019 (submitted herewith).

Even if the MSDS clearly established, as asserted in the Advisory Action, that the boiling point of the tetramethylammonium hydroxide compound, as opposed to the boiling point of methanol, is within 60-65°C, the melting point of tetramethylammonium hydroxide is still 63°C. How can the tetramethylammonium hydroxide compound have a boiling point that is below its melting point? Unless tetramethylammonium hydroxide is capable of sublimation under normal pressure, this would be impossible. Thus, either the MSDS is not referring to the boiling point of only the tetramethylammonium hydroxide compound, or it contradicts the Merck Index.

Even if it was agreed that the MSDS is referring to the boiling point of the solution of tetramethylammonium hydroxide and methanol, the rejection would still be improper. As discussed above, SPE Lorengo indicated that claim 1 does not exclude solutions. Nevertheless, Horie does not disclose tetramethylammonium hydroxide in solution. Instead, it discloses a suspension of 10 wt% diamond particles, 85 wt% pure water, and 5 wt% tetramethylammonium hydroxide (total content = 100 wt%). Horie does not disclose a solution of tetramethylammonium hydroxide and methanol. The rejection does not provide a reason or rationale as to why it would have been obvious to one of skill in the art to substitute the tetramethylammonium hydroxide compound of Horie with the tetramethylammonium hydroxide in methanol solution disclosed in Perry's MSDS.

Applicants respectfully submit that the Office Action fails to establish that the tetramethylammonium hydroxide compound of Horie has a boiling point of 50°C or higher and 300°C or lower as claimed. Hiraki and Perry's do not cure at least this deficiency.

Claim 1 would not have been rendered obvious by the combination of applied references. Claims 3 and 14-17 depend from claim 1 and, thus, also would not have been rendered obvious by the applied references. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

#### **VI. Rejoinder**

Applicants also respectfully request rejoinder of non-elected method claims 7 and 8. Where product and process claims are presented in the same application, Applicants may be called upon under 35 U.S.C. §121 to elect claims to either the product or process. MPEP §821.04. However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim. *Id.* Because process claims 7 and 8 include all the limitations of product claim 1, process claims 7 and 8 must be rejoined with the product claims when the product claims are found allowable. Because the product claims are believed to be allowable for at least the reasons presented above, Applicants respectfully request withdrawal of the Restriction Requirement and rejoinder of claims 7 and 8.

#### **VII. Conclusion**

In view of the foregoing, Applicants respectfully submit that this application is in condition for allowance. Applicants earnestly solicit favorable reconsideration and prompt allowance of the application.

Should the Examiner believe that anything further would be desirable to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



James A. Oliff  
Registration No. 27,075

Ryan R. Brady  
Registration No. 62,746

JAO:RRB/rrb

Attachment:

The Merck Index, 7<sup>th</sup> Ed., pp. 1018-1019

Date: August 17, 2009

**OLIFF & BERRIDGE, PLC**  
**P.O. Box 320850**  
**Alexandria, Virginia 22320-4850**  
**Telephone: (703) 836-6400**

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734 (1956); Wettstein *et al.*, U.S. pat. 2,900,398 (1959 to Ciba).

Crystals from acetone + ether. mp 163-164°.  $[\alpha]_D^{25}$  0° (c = 1.15 in chloroform). uv max: 245 nm ( $\epsilon$  15600).

Note: This is a controlled substance (anabolic steroid) in the U.S. Code of Federal Regulations, Title 21 Part 1308.13, as defined in Part 1308.02 (1995).

THERAP CAT: Androgen.

THERAP CAT (VET): Anabolic.

**6019. Methane.** Marsh gas; methyl hydride.  $\text{CH}_4$ ; mol wt 16.04. C 74.87%, H 25.13%. Widely distributed in nature. American natural gas is about 85% methane. The earth's atm contains 0.00022% by vol. Major constituent of the atm of the outer planets (Jupiter, Saturn, Uranus, Neptune), exact figures in *Landolt-Börnstein*, vol. III (Springer, 6th ed., 1952) p 59; G. P. Kuiper, *The Atmospheres of the Earth and the Planets* (University of Chicago Press, 1949). Pure carbon combines directly with pure hydrogen at temperatures above 1100° forming methane. Above 1500° amount of methane formed increases with temperature: Pring, *J. Chem. Soc.* 97, 498 (1910). Can be prepd from sodium acetate and sodium hydroxide, or from aluminum carbide and water: Matthews, *J. Am. Chem. Soc.* 21, 647 (1899); Carroll, *J. Phys. Chem.* 22, 148 (1918). Prepd commercially from natural gas or by fermentation of cellulose and sewage sludge: Cost, U.S. pat. 2,583,090 (1952 to Elliott Co.); Le Paige, de Dommartin, Fr. pat. 994,032 (1951), C.A. 51, 10836i (1957); Oswald, *Golueke, Mech. Eng.* 86, 40 (1964).

Colorless, odorless, non-poisonous, flammable gas. Burns with a pale, faintly luminous flame.  $d_4^{20}$  0.554 (air = 1) or 0.7168 g/liter. mp -182.6°. bp -161.4°. Crit temp -82.25°; crit pressure 45.8 atm. Heat of combustion 978 Btu/cu ft at 25° (a kilogram of  $\text{CH}_4$  yields 13,300 kcal). Forms explosive mixtures with air, the loudest explosions occur when one vol of methane is mixed with 10 vols of air (or 2 vols of oxygen). Air contg less than 5.3% methane no longer explodes. Air contg more than 14% methane burns without noise. Autoignition temp 650°. Soly in water at 17°: 3.5 ml/100 ml  $\text{H}_2\text{O}$ . Sol in alc, ether, other organic solvents.

Caution: Simple asphyxiant.

USE: Constituent of illuminating and cooking gas, in the manuf of hydrogen, hydrogen cyanide, ammonia, acetylene, formaldehyde, in organic syntheses.

**6020. Methanearsonic Acid.** *Methylarsonic acid*; methylarsinic acid; monomethylarsinic acid.  $\text{CH}_3\text{AsO}_3$ ; mol wt 139.97. C 8.58%, H 3.60%, As 53.53%, O 34.29%.  $\text{CH}_3\text{AsO}(\text{OH})_2$ . Prepd from sodium arsenite and methyl iodide: Quick, Adams, *J. Am. Chem. Soc.* 44, 809 (1922). The disodium salt is easily prepd by treating sodium arsenite with dimethyl sulfate at 85°: Uhlinger, Cook, *Ind. Eng. Chem.* 11, 105 (1919). Other routes are by the reaction of methyl chloride with sodium arsonate under pressure: Miller *et al.*, U.S. pat. 2,442,372 (1948); by the reaction of dimethyl sulfate with a solution of arsenic trioxide in sodium hydroxide: Schwerdtle, U.S. pat. 2,889,347 (1959). Acute toxicity: T. B. Gaines, R. E. Linder, *Fundam. Appl. Toxicol.* 7, 299 (1986).

Monoclinic, spear-shaped plates from abs alcohol. Pleasant acid taste. mp 161°. Strong dibasic acid. Freely sol in water; sol in alcohol.

Monosodium salt,  $\text{CH}_3\text{AsNaO}_3$ , *monosodium methanearsonate*, *MSMA*, *Ansar* 6.6, *Bueno*, *Daconate*, *Weed Hoe*.  $\text{LD}_{50}$  in adult male, female rats (mg/kg): 1105, 1059 orally (Gaines, Linder).

Disodium salt,  $\text{CH}_3\text{AsNa}_2\text{O}_3$ , *disodium monomethanearsonate*, *DSMA*, *Ansar* 8100, *Arrhenal*, *Arsinyl*, *Clout*, *Crab-E-Rad*, *Dal-E-Rad*, *Sodar*. Hydrated crystals contg  $5\text{H}_2\text{O}$  or  $6\text{H}_2\text{O}$ . One gram dissolves in about one ml water; slightly sol in alcohol.  $\text{LD}_{50}$  in adult male, female rats (mg/kg): 928, 821 orally (Gaines, Linder).

USE: Herbicide.

**6021. Methanesulfonic Acid.** *Methylsulfonic acid*.  $\text{CH}_3\text{SO}_3\text{H}$ ; mol wt 96.11. C 12.50%, H 4.20%, O 49.94%, S 33.36%.  $\text{CH}_3\text{SO}_3\text{OH}$ . Prepd from sulfur trioxide and methane: Snyder, Grosse, U.S. pat. 2,493,038 (1950 to Houdry Process); by oxidation of dimethyl disulfide: Johnson,

Wolff, U.S. pat. 2,697,722 (1954 to Standard Oil of Ind. ana); Proell *et al.*, *Ind. Eng. Chem.* 40, 1129 (1948). *Organic Chemistry of Sulfur* (Wiley, New York, 1944).

Solid.  $d_4^{18}$  1.4812. mp 20°. bp<sub>10</sub> 167°; bp<sub>1</sub> 122°. Soly in 26-28% in wt %: hexane, 0; methylcyclopentane, 0; benzene, 1.50; toluene, 0.38; o-chlorotoluene, 0.23; ethyl disulfide, 0.47. Thermally stable at moderately elevated temps. Not hydrolyzed by boiling water or hot aq alkali. Corrosive to iron, steel, brass, copper, lead.

Ethyl ester, see Ethyl Methanesulfonate.

Methyl ester, see Methyl Methanesulfonate.

Caution: Strong irritant.

USE: As catalyst in polymerization, alkylation and esterification reactions; as a solvent.

**6022. Methanesulfonyl Chloride.**  $\text{CH}_3\text{SO}_2\text{Cl}$ ; mol wt 114.55. C 10.49%, H 2.64%, Cl 30.95%, O 27.93%.  $\text{CH}_3\text{SO}_2\text{Cl}$ . Prepd from methanesulfonic acid and thionyl chloride: Hearst, Noller, *Org. Syn.*, coll. vol. IV, 571 (1963).

Liquid.  $d_4^{18}$  1.4805. bp<sub>30</sub> 161°; bp<sub>18</sub> 62°.  $n_D^{20}$  1.451. Practically insol in water; sol in alcohol, ether.

**6023. Methanethiol.** Methyl mercaptan; mercaptomethane; thiomethyl alcohol; methyl sulfhydrate.  $\text{CH}_3\text{SH}$ ; mol wt 48.11. C 24.97%, H 8.38%, S 66.65%.  $\text{CH}_3\text{SH}$ . Occurs in "sour" gas of W. Texas, in coal tar, and in petroleum distillates. Isolated from roots of *Raphanus sativus*. Produced in the intestinal tract by the action of anaerobic bacteria on albumin. Evolved from *Penicillium brevicatula* bread cultures containing disulfides. Prepn from sodium methyl sulfate and KHS: Klason, *Ber.* 20, 3409 (1887); Arndt, *ibid.* 54, 2236 (1921); catalytically from methanol and hydrogen sulfide: Kramer, Reid, *J. Am. Chem. Soc.* 44, 880 (1921); from methyl chloride and sodium hydrosulfide: Scott *et al.*, *Ind. Eng. Chem.* 47, 876 (1955). Toxicity data: *Handbook of Toxicology* vol. 1, W. S. Spector, Ed. (Saunders, Philadelphia, 1956) pp 344-345. Review on occurrence, preparation, properties and reactions: E. E. Reid, *Organic Chemistry of Bivalent Sulfur* vol. I (Chemical Publishing Co., New York, 1958) pp 15-261.

Flammable gas; odor of rotten cabbage. mp -135°. bp<sub>760</sub> 5.95°;  $d_4^{20}$  0.8665;  $d_4^{25}$  0.9600. Critical temp 196.1°. Critical pressure 71.4 atm. Heat capacity (solid at 14.9°: 146.57°K): 0.773-17.47 cal/deg/mole; (liq at 154.16-271.06°K): 21.27-21.13 cal/deg/mole, Russell *et al.*, *J. Am. Chem. Soc.* 64, 165 (1942). Azeotrope with isobutane (14.9% methanethiol) bp -13.00°. Soly in water at 27.23.30 g/l. Forms a cryst hydrate. LC for rats in air: 10000 ppm (Spector).

Sodium salt hemionahydrate,  $\text{CH}_3\text{SNa} \cdot 4\frac{1}{2}\text{H}_2\text{O}$ , needles. Freely sol in water, methanol. Practically insol in ether.

Copper salt,  $\text{CH}_3\text{SCu}$ , pale yellow crystals. Practically insol in water, ethanol, ether, benzene.

Caution: Potential symptoms of overexposure to methanethiol are narcosis; cyanosis; convulsions; pulmonary irritation. See *NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 90-117, 1990) p 154.

USE: Intermediate in manuf of jet fuels, pesticides, fungicides, plastics; synthesis of methionine.

**6024. Methanol.** Methyl alcohol; carbinol; wood spirit; wood alcohol.  $\text{CH}_3\text{OH}$ ; mol wt 32.04. C 37.48%, H 12.58%, O 49.93%.  $\text{CH}_3\text{OH}$ . Originally obtained by destructive distillation of wood, now usually manuf from hydrogen and carbon monoxide or carbon dioxide, also by oxidation of hydrocarbons. Review: Faith, Keyes & Clark's *Industrial Chemicals*, F. A. Lowenheim, M. K. Moran, Eds (Wiley-Interscience, New York, 4th ed., 1975) pp 524-529. L. E. Wade *et al.*, in *Kirk-Othmer Encyclopedia of Chemical Technology* vol. 15 (Wiley-Interscience, New York, 3rd ed., 1981) pp 398-415. Review of metabolism and toxicology: J. Liesivuori, H. Savolainen, *Pharmacol. Toxicol.* 69, 157-163 (1991).

Flammable, poisonous, mobile liq. Slight alcoholic odor when pure; crude material may have a repulsive, pungent odor. Burns with a non-luminous, bluish flame.  $d_4^{20}$  0.8100;  $d_4^{25}$  0.7960;  $d_4^{30}$  0.7915;  $d_4^{35}$  0.7866. mp -97.8°. bp<sub>10</sub> 64.7°; bp<sub>400</sub> 49.9°; bp<sub>200</sub> 34.8°; bp<sub>100</sub> 21.2°; bp<sub>60</sub> 12.1°; bp<sub>30</sub> 5.0°; bp<sub>20</sub> -6.0°; bp<sub>10</sub> -16.2°; bp<sub>5</sub> -25.3°; bp<sub>1</sub> -44.0°; bp<sub>0</sub> -50.0°.

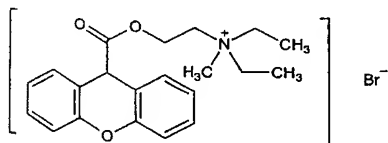


1.13066;  $n_D^{20}$  1.3292. Vapor density: 1.11 (air = 1). Flash pt., closed cup: 54°F (12°C). Ignition temp 470°C (878°F). Explosive limits (%-vol in air): 6.0 to 36.5. Crit temp 340.0°; crit pressure 78.5 atm. Specific heat at 20-25° = 0.593 to 0.605. Dipole moment 1.69. Miscible with water, ethanol, ether, benzene, ketones, and most other organic solvents. Forms azeotropes with many compds. Density, freezing and boiling point data of methanol-water mixtures: 10% methanol by vol ( $d_4^{25}$ , fp, bp): 0.9836, -5°, 92.8°; 20% methanol: 0.9695, -12°, 87.8°; 30% methanol: 0.9572, -21°, 84.0°; 40% methanol: 0.9423, -33°, 80.9°; 50% methanol: 0.9259, -47°, 78.3°; 60% methanol: 0.9082, -57°, 75.9°. Methanol usually is a better solvent than ethanol, dissolves many inorganic salts, e.g., sodium iodide 43%, calcium chloride 22%, ammonium nitrate 14%, copper sulfate 13%, silver nitrate 4%, ammonium chloride 3.2%, sodium chloride 1.4%.

**Caution:** Poisoning may occur from ingestion, inhalation or percutaneous absorption. **Acute Effects:** Headache, fatigue, nausea, visual impairment or complete blindness (may be permanent), acidosis, convulsions, mydriasis, circulatory collapse, respiratory failure, death. Death from ingestion of less than 30 ml has been reported. Usual fatal dose 100-250 ml. **Chronic:** Visual impairment, cf. Patty's *Industrial Hygiene and Toxicology* vol. 2C, G. D. Clayton, F. E. Clayton, Eds. (Wiley-Interscience, New York, 3rd ed., 1982) pp 4528-4541.

**USE:** Industrial solvent. Raw material for making formaldehyde and methyl esters of organic and inorganic acids. Antifreeze for automotive radiators and air brakes; ingredient of gasoline and diesel oil antifreezes. Octane booster in gasoline. As fuel for picnic stoves and soldering torches. Extractant for animal and vegetable oils. To denature ethanol. Softening agent for pyroxylin plastics. Solvent and solvent adjuvant for polymers. Solvent in the manuf of cholesterol, streptomycin, vitamins, hormones, and other pharmaceuticals.

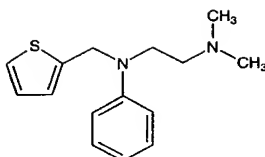
**6025. Methantheline Bromide.** *N,N*-Diethyl-*N*-methyl-1-[(9*H*-xanthen-9-ylcarbonyloxy)ethanaminium bromide; diethyl(2-hydroxyethyl)methylammonium bromide xanthene-9-carboxylate;  $\beta$ -diethylaminoethyl 9-xanthene-carboxylate methobromide; MTB-51; SC-2910; Banthine Bromide; Avalal; Uldumont; Vagantini; Metaxan; Methaniline; Xanteline; Gastron; Gastrosedan; Methanthine Bromide; Vagamin; Metanyl; Doladene; Asabaine.  $C_{27}H_{35}BrNO_3$ ; mol wt 420.35. C 60.01%, H 6.23%, Br 19.01%, N 3.33%, O 11.42%. Prepn from 9-xanthene-carboxylic acid and 2-diethylaminoethanol. J. W. Cusic, R. A. Robinson, *J. Org. Chem.* 16, 1921 (1951); *idem*, U.S. pat. 2,659,732 (1952 to Searle). Pharmacology: W. E. Hambourger *et al.*, *J. Pharmacol. Exp. Ther.* 99, 245 (1950).



Crystals from isopropanol, mp 175-176°. Bitter taste. Very slightly hygroscopic. Freely sol in water, alcohol. Practically insol in ether. pH (2% aq soln): 5.0-5.5. Aqueous solutions tend to hydrolyze after a few days. The corresponding chloride is very hygroscopic. uv max (alc): 246, 282 nm ( $E_{1\%}^{1cm}$  135, 69). LD<sub>50</sub> i.p. in mice: 76 mg/kg (Hambourger). THERAP CAT: Anticholinergic.

THERAP CAT (VET): Anticholinergic; antispasmodic; antisecretory agent.

**6026. Methaphenilene.** *N,N*-Dimethyl-*N'*-phenyl-*N'*-(2-thienylmethyl)-1,2-ethanediamine; *N,N*-dimethyl-*N'*-phenyl-*N'*-(2-thienyl)ethylenediamine; 00836; RP-2740; W-50 base; Diatrin base.  $C_{15}H_{20}N_2S$ ; mol wt 260.40. C 69.19%, H 7.74%, N 10.76%, S 12.31%. Prepd by a sodamide condensation of *N,N*-dimethyl-*N'*-phenylethylenediamine with 2-thienyl chloride in dry toluene: Leonard, Solmssen, *J. Am. Chem. Soc.* 70, 2066 (1948).

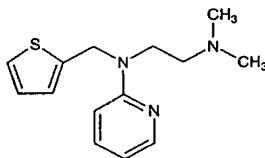


Dark yellow oil. bp, 183-185°.  $n_D^{25}$  1.5902. Hydrochloride,  $C_{15}H_{20}N_2S \cdot HCl$ , *Diatrin*, *Enstamine*, *Nilhistin*. Crystals from ethanol, mp 186-187°. Freely soluble in water. Soluble in alc. LD<sub>50</sub> i.p. in mice: 117 mg/kg.

THERAP CAT: Antihistaminic.

THERAP CAT (VET): Antihistaminic.

**6027. Methapyrilene.** *N,N*-Dimethyl-*N'*-(2-pyridinyl)-*N'*-(2-thienylmethyl)-1,2-ethanediamine; 2-[(2-dimethylaminoethyl)-2-thienylamino]pyridine; *N,N*-dimethyl-*N'*-(2-pyridyl)-*N'*-(2-thienyl)ethylenediamine; *N,N*-dimethyl-*N'*-( $\alpha$ -pyridyl)-*N'*-(2-methylthienyl)ethylenediamine; thienylpyramine; AH-42; Thienylene; Pyrrathyn; Semikon; Thionylan; Histadyl (formerly); Restyl; Rest-On; Sleepwell; Paradormalene; Pyrinistab; Pyrinistol; Lullamin.  $C_{14}H_{19}N_3S$ ; mol wt 261.39. C 64.33%, H 7.33%, N 16.08%, S 12.27%. Prepd by heating a 2-thienyl halide with an alkali metal salt of *N,N*-dimethyl-*N'*-(2-pyridyl)ethylenediamine: Kyrides, U.S. pat. 2,581,868 (1952 to Monsanto). Alternate syntheses: Weston, *J. Am. Chem. Soc.* 69, 980 (1947); Clapp *et al.*, *ibid.* 1549. Toxicity data: H. M. Lee *et al.*, *Proc. Soc. Exp. Biol. Med.* 80, 458 (1952). Carcinogenicity study: W. Lijinsky *et al.*, *Science* 209, 817 (1980). Study of mechanism of hepatocarcinogenicity: K. L. Steinmetz *et al.*, *Carcinogenesis* 9, 959 (1988). Clinical pharmacokinetics: E. P. Calandre *et al.*, *Clin. Pharmacol. Ther.* 29, 527 (1981). HPLC determin in feed and sleep aid tablets: B. Shaikh, M. R. Hallmark, *J. Assoc. Off. Anal. Chem.* 64, 889 (1981); in feed, urine and wastewater: H. C. Thompson, Jr., C. L. Holder, *J. Chromatog.* 283, 251 (1984).



Liquid. bp<sub>0.45</sub> 125-135°; bp<sub>3</sub> 173-175°.  $n_D^{25}$  1.5842 (also reported as 1.5835). LD<sub>50</sub> in mice, guinea pigs (mg/kg): 182.2  $\pm$  12.8, 374.9  $\pm$  34.5 orally; in mice (mg/kg): 19.85  $\pm$  0.69 i.v. (Lee).

Hydrochloride,  $C_{14}H_{19}N_3S \cdot HCl$ , bitter crystals, mp 162°. uv max: 238 nm ( $E_{1\%}^{1cm}$  623); min: 272 nm. One gram dissolves in about 0.5 ml water, in 5 ml alcohol, in 3 ml chloroform. Practically insol in ether, benzene.

Fumarate,  $(C_{14}H_{19}N_3S)_2 \cdot 3C_4H_4O_4$ . Prepn: Meyer, Brit. pat. 694,805 (1953 to Monsanto). Crystals, mp 135-136°.

THERAP CAT: Antihistaminic.

THERAP CAT (VET): Antihistaminic.

**6028. Methaqualone.** 2-Methyl-3-(2-methylphenyl)-4(3*H*)-quinazolinone; 2-methyl-3-*o*-tolyl-4(3*H*)-quinazolinone; 3,4-dihydro-2-methyl-4-oxo-3-*o*-tolylquinazolinone; metolquiazolone; MAOA; MTQ; ortonol; QZ-2; RIC-272; Rorer 148; TR-495; Cateudyl; Citexal; Dormigoa; Dormogen; Dormutil; Dorsedin; Fadormir; Holodorm; Hyminal; Hypcol; Hyptor; Ipnofil; Melsomin; Mequin; Mollinox; Motolon; Nobedorm; Noctilene; Normi-Nox; Omnyl; Optinoxan; Parminal; Parest; Quaalude; Roulone; Rouqualone; Sindesvel; Somnafac; Sonal; Somberol; Somnored; Soverin; Torinal; Tuazol; Tuazolone.  $C_{16}H_{14}N_2O$ ; mol wt 250.30. C 76.78%, H 5.64%, N 11.19%, O 6.39%. Prepn: Kacker, Zaheer, *J. Indian Chem. Soc.* 28, 344 (1951); Lab. Toraude, Brit. pat. 843,073 (1960); Klosa, *J. Prakt. Chem.* 14, 84 (1961); 20, 283 (1963). Improved synthesis: M. S. Manhas *et al.*, *Synthesis* 5, 309 (1977). Estimation in biol. materials: Akagi *et al.*, *Chem. Pharm. Bull.* 11, 62 (1963). Metabo-